Q79 Discussion of the papers by A. Boivin & Dr. Weil at
Cold Spring Harbor, June 17, 1947

1. My first remark concerns the alternative explanation of spontaneously occurring mutations to account for transformations. While the intuitive apprehensions of most of us, and of my self are such as to eliminate from our consideration this interpretation in this case, it has not been eliminated, nor indeed has any vigorous attempt been made to study it. Will a single S cell introduced amongst an R population manifest itself? This suggestion is not so much intended as a criticism of Dr. Boivin's conclusions, but as a general plea for the most scrupulous investigation of any system of mutagenesis, particularly where directed mutations are involved. This has not yet been done in our experiments with transformation, which I shall mention shortly.

2. Those of you who were present last year may recall the presentation of a paper by Professor Tatum and myself entitled "Novel Genotypes in Mixed Cultures of Bacterial Mutants" which dealt in as non-committal a fashion as we could develop with the appearance of so-called recombination types. We have since come to the conclusion that these types, in our strain, K-12 result from a sexual process of fusion rather than the transmission of transforming factors in the medium. Although I discussed this question in detail last night at an informal session, I hope you will forgive me if I summarize again very briefly the types of evidence which we have accumulated.

a. We have been unable to separate genetic or transforming activity from the living cell, either with extracts or filtrates or agar-diffusion procedures.

b. In mixtures of three genetic types, the only recombinants found are those which would result from the pairwise interaction of cells; there is thus no evidence of mixing of genetic materials in solution.

c. The presence of desoxyribonuclease, kindly provided by Dr. McCarty, in large doses has no effect on the yield of recombinants.

d. The analysis of 'crosses' in which the parents were heterozygous for a large number of different genetic factors (as many as eight) showed that the interchanges of various factors were quantitatively dependent on each other, but that all recombination classes could be recovered. This is to be distinguished by the absolute coupling of certain factors found by Weil, and can be simply interpreted in terms of a linkage and crossing over as in Drosophila.

e. The occurrence of all recombination classes implies that any transformations in this system would have to be capable of working in both directions.

While one could erect a formal theory explaining these results in terms of transformation, such a theory would be operationally indistinguishable, except for the hitherto unrealized possibility of chemical purification or cytological visualization from a situation in which genes are transmitted by a gamete, in which they are organized on a chromosome.

Unfortunately, the study of the biology of the transformations has not yet progressed to the study of the interactions of the transformations of independent factors, although perhaps Dr. Taylor might be induced to say a word about that.

In hopes of clarifying this problem, Dr. Boivin, Dr. Tatum and I are collaborating on a study of the S1-S2 system he has just described. Since his arrival in this country we have completed some preliminary experiments in which the transformation of a specific biochemical capacity seems to have taken place.

A mutant of S2 was obtained which is unable to decompose pyruvate according to the Lipmann reaction, and is therefore anaerogenic. (This mutant is designated Y109). The passage of Y109 through a filtrate or sterile extract of S1 has in at least 6/8 cases resulted in the production of a gas-producing strain, while spontaneous reversion of the mutant to gas production has not been noted in numerous controls. The transformed strains have not yet been examined serologically, but do retain their new biochemical capacity upon sub cultivation.

We are fully cognizant of the possibility of interpretations other than transformation, and cannot yet refute them. This information is presented as an illustration of the possible success of an approach comparable to that which was used in the "sexual' system which we have previously described, and in which we have been unable to induce any transformations with sterilized extracts.

It may be remembered that Dr. Sonneborn has pointed out that there are different hereditary organizations in different varieties of Paramecium; in some cytoplasmic inheritance plays a predominant role, while in others inheritance is strictly Mendelian.

---------- P.S. The Boivin system never worked out in our hands, and the strains disappeared from his. This was never published.